UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 15, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

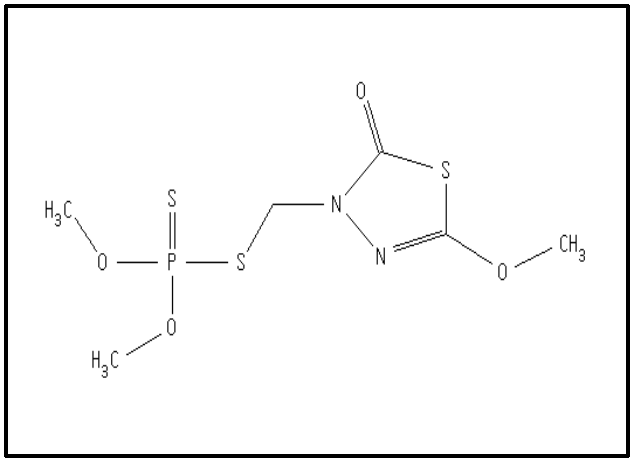
Jack E. Housenger, Acting Director
Special Review and Reregistration Division

TOXICOLOGY ENDPOINT SELECTION DOCUMENT

Chemical Name: Methidathion

PC Code: 100301

Structure:



Methidathion

The Health Effects Division Toxicology Endpoint Selection Committee considered the available toxicology data for Methidathion at a meeting held on June 4, 1996. Based upon a review of the toxicology database for the chemical listed above, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories below. A brief capsule of the study is presented for use in preparation of risk assessments.

Where no appropriate data have been identified or a risk assessment is not warranted, this is noted. Data required to describe the uncertainties in the risk assessment due to the toxicology database are presented. These include but are not limited to extrapolation from different time frames or conversions due to route differences. If route to route extrapolation is necessary, the data to perform this extrapolation are provided.

TOXICOLOGIST: MELBA S. MORROW Date: _____
(NAME)

SECTION HEAD: JOYCELYN E. STEWART Date: _____
(NAME)

BRANCH CHIEF: KARL P. BAETCKE Date: _____
(NAME)

DERMAL ABSORPTION DATA
No studies were available to assess the dermal absorption of methidathion. A 100% dermal absorption was assumed based on the results of a 21 day dermal toxicity study in rabbits in which systemic toxicity was reported at 1 mg/kg/day which represented the lowest dose tested. Systemic toxicity included mortality and clinical signs consistent with cholinesterase inhibition.

MRID: 40079806

% absorbed: assume 100 %
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ACUTE DIETARY ENDPOINT (ONE DAY)

Study Selected - Guideline No.: 82-7

MRID No.: 43582501

Summary: When methidathion was administered for 90 days in the diet to male and female Sprague Dawley rats at dose levels of 0, 3, 10, 30 or 100 ppm (equal to 0.2, 0.6, 1.9 or 6.3 mg/kg for males and 0.2, 0.7, 2.0 or 7.2 mg/kg for females), the compound was associated with effects on the FOB in females, only at levels which exceeded the LOEL for systemic toxicity. The NOEL was 3 ppm (0.2 mg/kg) and the LOEL was 10 ppm (0.6 mg/kg) based on statistically and biologically significant decreases in red blood cell, serum and central nervous system cholinesterase activity.

Endpoint and dose for use in risk assessment:
NOEL = 0.2 mg/kg/day based on decreases in serum (24%) and brain (26% decrease in cerebral cortex) cholinesterase activity at a two week measurement.

Comments about study and/or endpoint:
This NOEL and endpoint is supported by the NOEL of < 1.0 mg/kg observed in an acute neurotoxicity study in rats in which a 41% decrease in brain (cerebral cortex) cholinesterase activity was seen at 1.0 mg/kg/day after two weeks and cholinergic signs were seen at 4 mg/kg/day. The doses tested in the acute study were 0, 1, 4, 8 or 16 mg/kg.

This risk assessment is required.
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SHORT TERM-, INTERMEDIATE-, AND LONG-TERM OCCUPATIONAL OR RESIDENTIAL EXPOSURE

Study Selected - Guideline No.: 82-7

MRID No.: 43582501

Summary: When methidathion was administered for 90 days in the diet to male and female Sprague Dawley rats at dose levels of 0, 3, 10, 30 or 100 ppm (equal to 0.2, 0.6, 1.9 or 6.3 mg/kg for males and 0.2, 0.7, 2.0 or 7.2 mg/kg for females), the compound was associated with effects on the FOB in females, only at levels which exceeded the LOEL for systemic toxicity. The NOEL was 3 ppm (0.2 mg/kg) and the LOEL was 10 ppm (0.6 mg/kg) based on statistically and biologically significant decreases in red blood cell, serum and central nervous system cholinesterase activity.

Endpoint and dose for use in risk assessment:
NOEL = 0.2 mg/kg/day based on decreases in serum and regional brain cholinesterase activity at a two week measurement.

Comments about study and/or endpoint:
This NOEL and endpoint is supported by the NOEL for cholinesterase inhibition of 1.0 mg/kg observed in a 21 day dermal study. In this study, males exhibited decreases in plasma, red cell and brain cholinesterase activity and females exhibited decreases in red cell and brain cholinesterase activity at the LOEL of 10.0 mg/kg/day. Although the study was classified as supplementary due to a lack of a systemic NOEL, it can be upgraded based on criteria developed during the rejection rate analysis which stated that the lack of a NOEL and the use of an occlusive bandage would not be sufficient reasons to reject a dermel toxicity study.

This risk assessment is required.

INTERMEDIATE

Summary: See Acute dietary

Endpoint and dose for use in risk assessment:
NOEL = 0.2 mg/kg/day based decreases in cholinesterase activity at a two week measurement.

Comments about study and/or endpoint:
This NOEL and endpoint is supported by the cholinesterase NOEL of 1.0 mg/kg observed in a 21 day dermal study. In this study, males exhibited decreases in plasma, red cell and brain cholinesterase activity and females exhibited decreases in red cell and brain cholinesterase activity at the LOEL of 10.0 mg/kg/day. Although the study was classified as supplementary due to a lack of a systemic NOEL, it can be upgraded based on criteria developed during the rejection rate analysis.

This risk assessment is required.

CHRONIC

Summary: In a one year chronic dog study, methidathion was administered at oral doses of 0, 0.5, 2.0, 4.0, 40.0 or 140 ppm/day. This is equivalent to a mg/kg/day dose of 0, 0.02, 0.07,

0.15, 1.33 or 4.51 for males and 0, 0.02, 0.07, 0.15, 1.39 or 4.9 for females. The NOEL in this study was 4 ppm (0.15) mg/kg/day for both sexes based on elevation of hepatic enzymes, gross hepatic lesions and microscopic presence of bile plugs, distended bile canaliculi and chronic hepatitis, all occuring at 40 ppm (1.33 mg/kg). At the LOEL of 40 ppm, erythrocyte cholinesterase activity was significantly decreased.

Dose and Endpoint: NOEL = 0.15 mg/kg/day based on liver pathology as discussed in the above summary and on erythrocyte cholinesterase depression.

Comments about dose/study: This study was used to establish the RfD.

This risk assessment is required.
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INHALATION EXPOSURE (ANY TIME PERIOD):
A waiver was granted for an acute inhalation study with the technical product. A 50% formulation product (Supracide 50S) was placed in Toxicity category I with an LC50 of 0.0106 mg/L in males and 0.00111 mg/L in females. Toxic signs and necropsy revealed a strong irritation potential in the respiratory, circulatory, excretory, nervous and gastrointestinal systems.

For the risk assessment, the inhalation and dermal components should be added together in the calculation of the mixer, loader, applicator estimates of exposure. The percent absorption for inhalation should be 100% (default value).

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ACUTE TOXICITY ENDPOINTS:

Acute Toxicity of Methidathion

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral	00139328	LD_{50} > 46.1 mg/kg	II
81-2	Acute Dermal	00139326	LD_{50} > 1663 mg/kg	II
81-3	Acute Inhalation	waived	waived	waived
81-4	Primary Eye Irritation	00159199	mild irritant	III
81-5	Primary Skin Irritation	00159200	Non-irritant	IV
81-6	Dermal Sensitization	252433	non-sensitizer	N/A
81-8	Acute Neurotoxicity	43145903 43590304	NOEL < 1mg/kg	neurotoxicant